Application No.: 10/084,706 Attorney Docket No: 0228us410

Preliminary Amendment dated Mar. 7, 2003

Page 3 of 8

Listing of Claims:

The following listing of claims replaces all prior versions and listings of claims in the application:

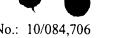
1.-87. (Canceled)

- 88. (New) An interferon β polypeptide variant exhibiting interferon β activity, comprising a variant sequence which differs from the wild-type human interferon β sequence SEQ ID NO:2 in no more than 15 amino acid residues, the variant sequence comprising (a) at least one N-glycosylation site and (b) an amino acid substitution at position –1 relative to at least one of the N-glycosylation site(s).
- 89. (New) The variant according to claim 88, wherein at least one of the N-glycosylation site(s) is a naturally occurring N-glycosylation site.
- 90. (New) The variant according to claim 88, wherein at least one of the N-glycosylation site(s) is an introduced N-glycosylation site.
- 91. (New) The variant according to claim 90, wherein the introduced N-glycosylation site is in a position that in wild-type human interferon β is occupied by an amino acid residue having at least 25% of its side chain exposed to the solvent.
- 92 (New) The variant according to claim 90, wherein the variant comprises at least two introduced N-glycosylation sites.
- 93. (New) The variant according to claim 92, comprising an amino acid substitution at position -1 relative to at least one of the introduced N-glycosylation site(s).

Application No.: 10/084,706 Attorney Docket No: 0228us410 Preliminary Amendment dated Mar. 7, 2003 Page 4 of 8

94. (New) The variant according to claim 88, further comprising at least one non-polypeptide moiety covalently attached to the variant.

- 95. (New) The variant according to claim 94, comprising at least one sugar moiety and at least one polymer molecule.
- 96. (New) The variant according to claim 95, wherein at least one of the polymer molecule(s) is covalently attached to a lysine residue of the variant.
- 97. (New) The variant according to claim 95, wherein at least one of the polymer molecule(s) is covalently attached to the N-terminus of the variant.
- 98. (New) The variant according to claim 95, wherein the polymer molecule comprises a linear polyethylene glycol or a branched polyethylene glycol.
- 99. (New) A composition comprising the variant of claim 88 or 94 and a pharmaceutically acceptable diluent, carrier, or excipient.
- 100. (New) A nucleic acid comprising a nucleotide sequence encoding the variant of claim 88.
- 101. (New) An expression vector comprising the nucleic acid of claim 100.
- 102. (New) A glycosylating host cell comprising the expression vector of claim 101.
- consisting of an *S. cerevisiae* cell, a *Pichia pastoris* cell, a CHO cell, a BHK cell, an HEK cell and an SF9 cell.



Application No.: 10/084,706 Attorney Docket No: 0228us410

Preliminary Amendment dated Mar. 7, 2003

Page 5 of 8

104. (New) A method of making a variant, the method comprising: providing a culture comprising a glycosylating host cell, the glycosylating host cell comprising a nucleotide sequence which encodes the variant of claim 88, culturing the culture under conditions which permit expression and glycosylation of the variant, and recovering the variant.

- 105. (New) The method according to claim 104, wherein the glycosylating host cell is selected from the group consisting of an *S. cerevisiae* cell, a *Pichia pastoris* cell, a CHO cell, a BHK cell, an HEK cell and an SF9 cell.
- 106. (New) The method according to claim 104, further comprising attaching at least one non-polypeptide moiety to the variant, wherein the non-polypeptide moiety comprises a polymer molecule.
- 107. (New) The method according to claim 106, wherein the polymer molecule comprises a linear polyethylene glycol or a branched polyethylene glycol.
- 108. (New) A method for producing a variant IFNB molecule exhibiting increased *in vivo* N-glycosylation relative to a parent IFNB molecule, the parent IFNB molecule comprising a parent IFNB sequence comprising at least one N-glycosylation site, which method comprises:
 - introducing a mutation into a parent polynucleotide that encodes the parent IFNB sequence, to produce a variant polynucleotide that encodes a variant IFNB sequence, the mutation introducing into the variant IFNB sequence an amino acid substitution at position –1 relative to at least one of the N-glycosylation site(s) of the parent IFNB sequence,
 - expressing the variant polynucleotide to produce the variant IFNB molecule, and the parent IFNB polynucleotide to produce the parent IFNB molecule, in glycosylating host cell cultures under comparable conditions,
 - iii) comparing the degree of glycosylation of the variant IFNB molecule and the parent IFNB molecule, and



Application No.: 10/084,706 Attorney Docket No: 0228us410

Preliminary Amendment dated Mar. 7, 2003

Page 6 of 8

iv) if necessary, repeating steps i) and ii), each time substituting a different amino acid at position -1 into the variant IFNB sequence, until a variant IFNB molecule exhibiting increased *in vivo* N-glycosylation relative to the parent IFNB molecule is obtained.